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KENYON & KENYON LLP
ONE BROADWAY
NEW YORK, NY 10004

EXAMINER	
CHANG, CELIA C	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/661,259	DOLITZKY ET AL.	
	Examiner	Art Unit	
	Celia Chang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on /.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-10,121 and 123-130 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-10,121 and 123-130 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This application is a RCE of SN 10/661,259.

Claims 11-120, 122, 131 have been canceled. Claims 1-10, 121, 123-130 are pending.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 3 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

There is no antecedent basis for the upper and lower layer yet one layer has a volume negligible compare to the volume of the other layer. The amendment in the two claims are self conflicting because if two layers are formed, they must have substantial volume of each layer. One can be less than the other but not "negligible" since such cannot be a two layer system.

Removal of new matter is required. In re Russmussan 210 USPQ 325.

3. Claims 6-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kumar et al. WO 00/71124 (recited on 1449) in view of Hackh's Liberman, Sekiguchi or Leucuta.

Determination of the scope and content of the prior art (MPEP §2141.01)

Kumar et al. '124 disclosed process for preparation of amorphous fexofenadine hydrochloride which anticipated the basic steps of the claims see examples 1-5.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between Kumar et al. and the instant claims is that an trituration step was added after preparation of amorphous form, a trituration step was carried out. Hackh's chemical dictionary defined that trituration is a grinding of particles or a size reduction procedure. Sekiguchi disclosed advantages of wet milling suitable for pharmaceutics for size reduction. Liberman taught that size reduction in pharmaceutics is desirable since the smaller particle size will have formulation advantages (see p.110-111) and such effect has been evidenced in pharmaceutical products (see Leucuta).

Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)

One having ordinary skill in the art would be aware of all the relevant art in the pharmaceutical size reduction and formulation field. The above reference placed the motivation of size reduction, the reasonable success of size reduction by trituration, and the expected advantage in formulation in the possession of one having ordinary skill in the art. The addition of a conventional size reduction step in a proven process is prima facie obvious.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-10, 121, 123-130 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kumar et al. WO 00/71124 in view of Hackh's Liberman, Sekiguchi or Leucuta , further in view of Okabe et al. CA 114:54120 or Williams et al. US 6,862,890.

Determination of the scope and content of the prior art (MPEP §2141.01)

Kumar et al. '124 disclosed process of making the amorphous product of the claims by spray drying of fexofenadine hydrochloride solution of organic solvents which has been established to be prima facie obvious supra and incorporated by reference.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the currently amended process and the prior art process of obtaining amorphous fexofenadine hydrochloride is that the claims are limited to the particular solvent THF or evaporation process for solvent removal.

Okabe et al. CA 114 disclosed that both spray dryer and evaporator are alternative apparatus for solvent removal. Williams et al. '890 taught that in pharmaceutical particulation

processes of fexofenadine hydrochloride (see col. 15 line 39), spray drying is a solvent removal procedure analogous to other conventional solvent removing procedures (see col. 1 lines 26-27, col. 2 lines 59-60) and optionally ethanol, methanol or tetrhydrofuran are choices of solvents (see col. 4 lines 51-56).

Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)

On having ordinary skill in the art in possession of the above references are in possession of the claims **because** Kumar et al. disclosed proven process of obtaining amorphous fexofenadine hydrochloride from solution by solvent removing and Williams or Okabe taught the proven interchangeability among the different solvents and solvent removing techniques conventional in the art. In absence of unexpected results, there is nothing unobvious in picking certain solvent or solvent removing choice among the proven operable alternatives.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-10, 121-131 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carr et al. US 4,254,129, 4,285,957, or WO 95/31437 (all cited on 1449) or Woosley Us 5,375,693 in view of Lieberman, Suzuki et al. CA 91:44479, Corrigan et al. CA 98:166814, Nuernberg CA 86:8603 and Sato CA 110:179429 supplemented with US 5,990,127.

Determination of the scope and content of the prior art (MPEP §2141.01)

The primary references disclosed fexofenadine hydrochloride:

See Carr '129, col. 13, example 3,
Carr '957 col. 13, example 3
WO 95/31429 claims 10-11, 13-15, 17-19, p. 11 lines 22-29 solvents
Woosley et al. '693, col. 10, example 1B, and solvent.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the prior art and the instant claims is that the amorphous form or process of spray dry or evaporation or triturating etc. for preparing an amorphous form was not explicitly disclosed. However, Lieberman, Suzuki, Corrigan, Nuernberg or Sato provided perponderous of evidence that spray drying or evaporation or trituration processes are size reduction processes for pharmaceutical products and such size reduction would enhance drug dissolution thus bioavailability (see Lieberman).

Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)

One having ordinary skill in the art in possession of the above references would be motivated to prepare the amorphous form of the drug **because** process of preparing the named compound is conventionally explicitly taught using the claimed solvents. One skilled in the art

would be motivated to carry out the prior art process employing spray drying, evaporation or trituration since it was clearly suggested by the prior art that spray drying, evaporation or trituration or combination thereof are size reduction routine procedure in formulation which enhances drug dissolution, also such process would inherently produce the amorphous form. Further, the claimed product, when prepared from a biological resource, has been prepared routinely employing the procedure lyphiolization which is solvent removal, supplied evidence that solvent removal are routine procedure in drug formulation.

6. The gist of applicants' arguments with respect to the 103(a) rejections in the parent applications are:

(i) there are other steps in the claim, therefore, the sole difference between the claims and the prior art is not spray drying vs evaporation.

Please note that the other steps in claim 1 is "preparing a solution, removing a portion of the solvent, adding another solvent, when two layer forms, separate the two layers". This adding one solvent, adding another immiscible solvent so that two layer forms to separate the lower layer is clearly known conventionally in the chemical art as "extraction" process. Please note that whether the fexofenadine hydrochloride was dissolved in one solvent or extracted into another solvent, such steps are the preparation step of solution making conventional in the chemical art. The Kumar '124 reference on pages 4-5 delineated preparation of solution. The Williams '890 reference taught that spray drying is solvent removal procedure analogous to other conventional solvent removing procedures (see col. 1, lines 26-27, col. 2 lines 59-60) and particularly taught the equivalency between applicants tetrahydrofuran and other alcohols such as those used by Kumar '124. Okabe et al. is further evidence that such analogue between spray drying and evaporation is a broad spectrum approach per ponderously conventional in the industry in amorphous solid preparation.

Attorney's attempt to show unobviousness by comparing only the difference of *each individual* reference instead of the combination of well-known analogous art in the field does not warrant any probative value. In re Merck & Co. 231 USPQ 375, Ex parte GPAC Inc. 29 USPQ2d 1406. Please note both Kumar and Williams have particularly "named" applicants compound and the all three references are for "solid amorphous" product procedure, thus, all are analogous art. Although the Okabe reference was recited as an example of the well known nature between spray drying and *rotary* drying, per ponderous of evidence in the pharmaceutical art support the analogue, see for example CA 139:219273, CA 113:120830, CA 138:390718, CA 141:179642, which are just a brief browsing of the most recent publication.

Applicants further argued that newly amended step in claims 6 and 125 of "triturating" which also differ from the prior art. On page 9 of the specification, it has clearly disclosed that trituration is an optional step further made "after" an amorphous form was received. The addition of an conventional size reduction step may obviate anticipation but does not obviate the obviousness see supra new ground of rejection necessitated by applicants amendment.

(ii) polymorphism is unpredictable. Please note that any unpredictability in the field of polymorphism has absolutely no relevancy on the instant claims which are *amorphous* products.

The Wikipedia encyclopedia is hereby attached for applicant's convenience. Please note that the definition of polymorphism strictly is for "crystal structure" . Amorphous is **not** crystal. Any unpredictability in crystal structure has no relevancy on amorphous because they are predictable and stable as Lieberman of record has taught. Even if there are unpredictable factors in obtaining "multiple" crystalline forms for a known crystal, the encyclopedia clearly provided evidence that just because there are many factors to be considered thus is time consuming, such process of multiple crystalline form is not unpredictable but proportional to the time and money one is willing to spend on such project.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (g)(1) during the course of an interference conducted under section 135 or section 291, another inventor involved therein establishes, to the extent permitted in section 104, that before such person's invention thereof the invention was made by such other inventor and not abandoned, suppressed, or concealed, or (2) before such person's invention thereof, the invention was made in this country by another inventor who had not abandoned, suppressed, or concealed it. In determining priority of invention under this subsection, there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other.

Claims 1-10, 121,, 123-130 are provisionally rejected under 35 U.S.C. 102(e) or (g) as being anticipated by US 2005/0165056.

See page 2, examples 5-6 and page 3 claims 15-19.

This is a provisional rejection since the claims or the pre-grant publication has not yet been patented. Please note that the Kirsch pre-grant publication is entitle to priority benefit of a NAFTA country.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

OACS/Chang
May 22, 2007-05-23

Celia Chang
Primary Examiner
Art Unit 1625